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ECIS Z θ

Electric Cell-substrate Impedance Sensing

Redefining the cell-based assay!

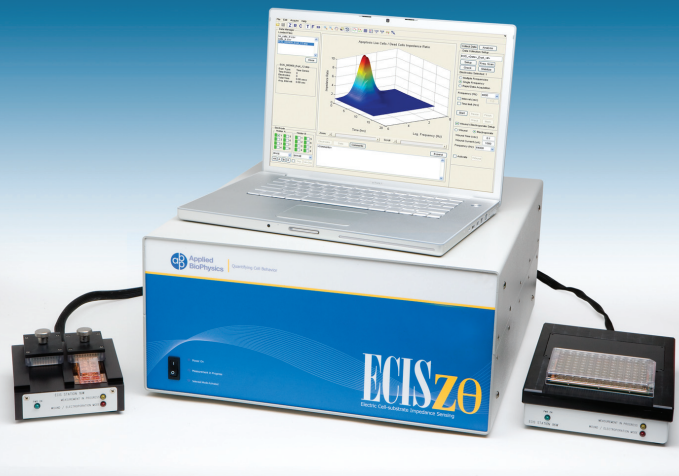
The ECIS Z θ (theta) is a turnkey system that provides researchers with an advanced, automated, non-invasive means to monitor cell behavior in real-time and without the use of labels.

ECIS measures the complex impedance of small 250-micrometer diameter electrodes used as substrates for cell growth. As cells grow on the electrode they constrict current flow altering the impedance. The ECIS Z θ reliably monitors up to 16 or 96 tissue culture wells. ECIS Z θ interprets the complex impedance as both resistance and capacitance and can report these values as well as the simple impedance.

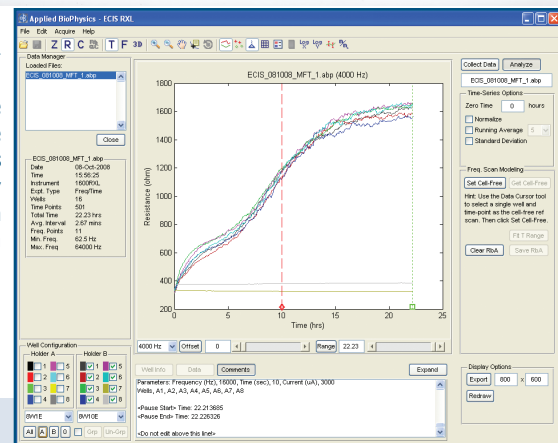
Using a mathematical model the system can report time courses changes in the barrier function (permeability) of confluent cell layers as well as membrane capacitance and a term (α) related to the close contacts between the cell's basal membrane and substrate. Other instruments that measure TER are designed for tight epithelial layers. ECIS is not limited to these layers and has proved particularly useful for studying endothelial cell layers with continuously and in real time.

The ECIS Z θ consists of a system controller, 16 and/or 96 well station, arrays, computer; integrated software runs on XP, Vista or Mac OS. Accessories include an optional flow module for specialized cell applications under flow conditions as well as an elevated field module to carry out automated wound-healing and electroporation experiments.

Fast • Reliable • Reproducible • Highly sensitive
• Quantitative • Accurate • Real-time



New, user-friendly, software interface allows versatility for data acquisition and analysis.

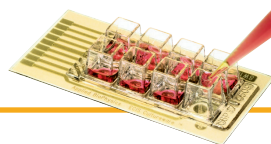


Published Application Include:

- | | |
|------------------------|------------------|
| Barrier Function | Motility |
| Permeability | Angiogenesis |
| Signal Transduction | Proliferation |
| Wound-healing | Apoptosis |
| Electroporation | Cell Growth |
| Cell Migration | Cells Under Flow |
| Extravasation | ECM Interactions |
| Cytopathic effects | Cytotoxicity |
| Cell-Cell Interactions | Chemotaxis |

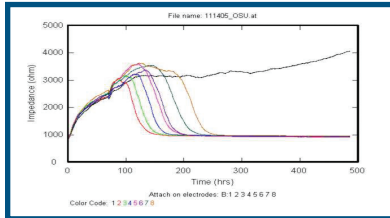


Quantifying Cell Behavior



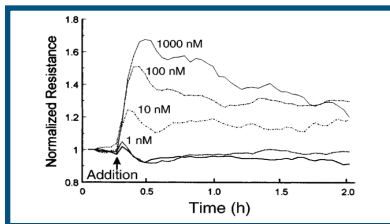
Data Output

Z v. T: Impedance v. Time



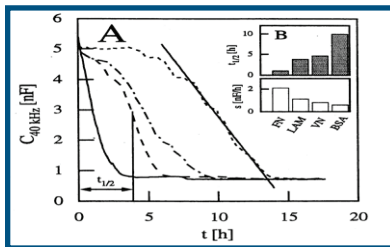
Used for general morphological changes in cells. Response of cells to viral infection is shown.¹

R v. T: Resistance v. Time



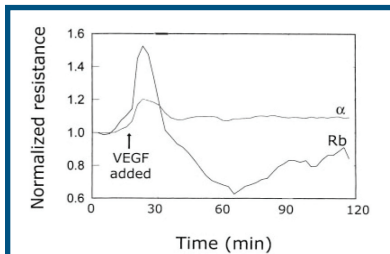
Used for general morphological changes in cells. Also used to quickly measure cell-cell interaction. Left, data showing dose response of BPAEC cells to Sph-1-P or thrombin.²

Rb Data



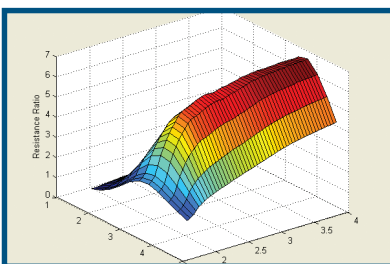
Mathematical modeling can be called up to monitoring changes in barrier function as shown above following the addition of VEGF to endothelial cells.³

C v. T: Capacitance v. Time



Monitoring the dynamics of cell attachment & spreading. Capacitance plots are also used to determine and measure cell confluence and proliferation.⁴

3D Data: Resistance v. Frequency v. Time



3D plots allow researchers to visualize time course data at multiple frequencies providing a third axis of analysis for informative trend observation.⁵

1: Z v. T: Courtesy of Dr. Ivar Giaever, Applied BioPhysics.

2: R v. T: Garcia, J.G.N., Liu, F., Verin, A.D., Birukova, A., Dechert, M.A., Gerthoffer, W.T., Bamberg, J.R., English, D., "Sphingosine 1-phosphate promotes endothelial cell barrier integrity by Edg-dependent cytoskeletal rearrangement" *J Clin Invest.* 108(5): 689-701, (2001).

3: C v. T: Wegener, Joachim, Keese, R., Charles, Giaever, Ivar, "Electric Cell-Substrate Impedance Sensing (ECIS) as a Noninvasive Means to Monitor the Kinetics of Cell Spreading to Artificial Surfaces" *Experimental Cell Research* 259, 158-166 (2000).

4: Rb Data: Becker, Patrice M., Verin, Alexander D., Booth, Mary Ann, Liu, Feng, Birukova, Anna and Garcia, Joe G. N., "Differential regulation of diverse physiological responses to VEGF in pulmonary endothelial cells", *Amer J. Physiol.*, 281: L1500-L1511, (2001).

5: 3D Plot: Courtesy of Dr. Charles Keese, Applied BioPhysics.

Instrument Features:

Array Stations

- 16 or 96 wells station option
- 16 well station accepts any combination of two 8 well arrays

Experiment Setup

- Quick well check confirms electrical connection
- Electrode stabilization cleans and prepares electrodes for measurement

Data Acquisition

- Continuous multiple frequencies over time (11 preset frequencies)
- Continuous single frequency over time (frequency variable from 50 to 100k Hz)
- Rapid time collection
 - Single frequency - up to 5 points per second
 - Multiple frequency - 10 seconds per well
- User specified time interval between data points
- User specified time limit on data collection
- Automatic file name generation
- All experiment parameters & operations automatically recorded in data files

Data Analysis

- Analyze data while data collection is in progress
- Export data to CSV for easy import to Excel etc (Excel is included with systems)
- Open and analyze multiple data sets
- Import CSV files from previous ECIS software

Graphing Options:

- Interactive pan, zoom, data cursor
- Lines, points or both (2D)
- Grid lines, Legend
- Logarithmic X or Y axes (2D)
- Time Marks indicating (Wound, Pause, User Mark)
- 3D plotting of multiple frequency time course data
 - Surface lines, shading or both
 - Interactive graph rotation
 - Color bar (for surface plots)

Graph Views: (15 variations)

- Z, R, C, v. time
- Z, R, C, v. frequency
- Multiple wells over time
- Single well 3D surface, time v. freq. v. Z, R, C

Data Processing Options:

- Normalize across multiple wells
- Running average
- Standard deviation
- Grouping of multiple wells (averaged)
- Optional standard deviation error bars of grouped data
- User defined time offset

Data Modeling for Barrier Function:

- Plot Cell and Cell-free Frequency scans
- Plot Cell/Cell-free ratio in 2D or 3D
- Fast fitting of model parameters to frequency scan data
- Fit single time point or time series
- Plot Rb, Alpha, Cell membrane capacitance
- Export data as .csv, easy import to Excel (incl with ECIS)
- Ability to Model multi-frequency data

Graph Export Options:

- User defined size
- Copy to clipboard (PC only)
- Save graph as 13 file types: .mat, .ai, .bmp, .eps, .emf, .jpg, .pcx, .pdf, .pbm, .pgm, .ppm, .pkm, .tif